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THE TREATMENT OF TETANUS WITH COLLIDON (PERISTON-N)

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[Numbers in parentheses refer to appended bibliography.]

The classical treatment of acute clinical tetanus entails a very high lethality. Thus, Huebner (Berlin) reported in 1954 on 1,894 cases, of which 930 (50 percent) had a lethal outcome. (1) Passive serum-prophylaxis was used in these cases. Huebner rightly recommends active prophylactic inoculations on the basis of favorable results obtained by the Allied Armies in World War II. Huebner mentions that more children die of tetanus in West Germany than of diphtheria. This high lethality is also confirmed by our experience during the period 1945-1953 when, of 31 patients treated by us, 13 (a lethality ratio of 42 percent) died.

As far as the new methods of therapy with curariform drugs or artificial hibernation are concerned, we were hitherto not in a position to apply them. Up to 1953, we had to be content with the old methods of thorough surgical treatment of the wounds (Prof Dr Kaestner), administration of high doses of antitoxic serum, keeping patients in a room protected from light and noise, and administration of high doses of penicillin, chloral hydrate, and barbiturates.

A new way of treatment was suggested by Bennhold's work, at his Tuebinger clinic, on the carrier functions fulfilled by natural (physiological) and synthetic colloids (2), and particularly by the concepts developed by his collaborator, Schubert [Dr Rene Schubert of the University Medical Clinic and Polyclinic, Tuebingen, West Germany], in regard to the detoxifying activity of Periston-N. (3)

Because of its pronounced capacity to retain water, Periston-N was originally used as a blood substitute following heavy blood losses. (4) In addition to a mixture of physiological salts, periston contains the synthetic colloid collidon (kollidon), i.e., polyvinylpyrollidone synthesized according to Reppe.

Periston-N is a collidon which has a low molecular weight of 12,600. Polyvinylpyrollidone of any desired molecular weight can be synthesized. The periston used as a plasma substitute has an average molecular weight of 50,000 and a molecular weight range of 10,000-80,000.

In 1944, Bennhold and Schubert discovered the so-called embatic activity of collidon. While Congo red does not diffuse from an ordinary aqueous solution into a layer of gelatin superimposed on this solution, it does diffuse into the gelatin when the solution contains 0.5% of collidon. In relation to bacterial toxins, snake poisons, and barbiturates, collidon exerts a vehicle or carrier action, similar to that discovered by Bennhold with reference to blood proteins. This property of collidon induced Bennhold to draw a parallel between blood plasma and periston, and to speak on the resemblance of periston to blood plasma in that respect. The low-molecular fractions of collidon pass readily through the kidneys and are eliminated with the urine.

With particular reference to tetanus, Schubert developed the following ideas, which were confirmed by relevant model experiments and experiments carried out on animals.

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Like many other bacterial toxins, the toxin of tetanus is bound by globulin without being detoxified and is transported to the nerve cells in that state. If collidon is added to the serum, the toxin is distributed between the serum proteins and the collidon in such a manner that an equilibrium is established. However, the toxin bound to the collidon is detoxified by the latter, just as it would have been detoxified by antitoxin, and is then eliminated through the kidneys. In order to understand the problem which is involved in the therapy of tetanus, one must consider the relative dimensions of the tetanus toxin, antitoxin, and collidon (Periston-N). While the toxin, which has a molecular weight of 70,000, can penetrate into the nerve cells producing clinical manifestations of tetanus, the antitoxin, which has a molecular weight of 170,000 or higher, cannot penetrate into these cells because of its large size. Consequently, the antitoxin is capable of exerting its neutralizing action in the serum only.

The situation is different with reference to Periston-N. Because of its low molecular weight, the periston penetrates into the cells where it comes into cantact with the toxin, detoxifies the latter, and transports it through the kidneys into the urine. This "washing of the cells" has been demonstrated by Schubert in work on guinea pigs and mice poisoned with toxin. The fact that detoxification with periston takes place, has been definitely confirmed in Schubert's experiments by a statistical treatment of the data. The appearance [of the toxin] in the urine of poisoned animals after collidon has been administered (the same phenomenon was observed by Dieckhoff in the case of diphtheria toxin) lent further support to Schubert's ideas on the subject. The therapeutic value of collidon (Periston-N) consists, on the one hand, in its hemodynamic activity (binding of water, increase of volume, and increase of osmotic pressure) and, on the other hand, in its adsorptive capacity and capacity to be eliminated with the urine. In other words, it carries detoxification into the cells and brings about purification of the cells, serum, and tissues as postulated by Schubert.

The transfer of the results of animal experiments and of serological tests to human beings, and the successful therapeutic application of these results, have hitherto been effected on only one occasion. (3) Under the circumstances, further confirmation of the conclusions reached with respect to tetanus is needed.

Since we began to use Periston-N in the fall of 1953, we have not lost a single patient, but cured all of them, without exception. The number of patients treated was five. One may raise the objection that this is too small a number of cases for a statistically valid result. Nevertheless, the results obtained by us must still be regarded as significant, because of the high lethality which is generally encountered in tetanus. There is the added circumstance that many, but very acute, endemic outbreaks of tetanus have taken place in Saxony during recent years. Moerl and Richter lost all of the eight patients in succession whom they had treated in Leipzig and lost 17 patients out of 33 during 1920-49. (5) Of the nine patients treated by Heinze in Karl-Marx-Stadt [GDR], only 5 survived. (6)

Among the five patients saved by us there were acute cases accompanied by early tetany, an opisthotonus of a very rigid type, and violent stretching spasms.

Because our confidence in the therapeutic effectiveness of collidon had increased, we reduced the doses of antitoxic serum from 500,000-1,000,000 units to 50,000-60,000 units in the last two cases treated. We had no deaths due to serum shock of the type described by Kuntzen (7), because we never introduced serum intravenously. Severe allergic serum reactions affecting the skin, the mucous membranes, and the joints, could be controlled by administering an antihistaminic drug. Very high temperatures are reduced when treatment with serum is stopped, while moderate fever is alleviated when administration of penicillin is also terminated.

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We administered penicillin to prevent the possible development of pneumonia.

We are of the opinion that with higher doses of Periston-N it will be possible to omit administration of the serum altogether. We experienced difficulties in procuring Periston-N [and for that reason were unable to apply sufficiently high doses of the drug]. The effectiveness of the administration of antitoxic serum after tetanus had set in, is questionable. In many cases the serum exerts no effect, even if it has been applied on time, as a prophylactic.(7)

We wish to add that we also obtained striking results by treating individual cases of other acute toxic infections besides tetanus with Periston-N. This refers to a case of severe edematous diphtheria and a cholera nostras infection, accompanied by a collapse of circulation which endangered the patient's life. Similar beneficial results were obtained by our pediatrician, Dr Breyer-Pueschel, in treating toxicosis of infants with Periston-N.

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